## REMARKS

I. INTRODUCTION

In response to the Office Action dated July 23, 2008, withdrawn claims 38 and 46-49 have been cancelled and claims 36 and 37 have been amended. Claims 26-37, 39-45 and 50 remain in the application. Re-examination and re-consideration of the application, as amended, is requested.

II. CLAIM AMENDMENTS

Minor amendments were made to claims 36 and 37 in order to correct typographical errors.

III. CLAIM OBJECTIONS

On page 2 of the Office Action, claims 36 was objected to due to a typographical error. In response to this objection, claim 36 has been amended.

IV. REJECTION UNDER 35 U.S.C. §112, FIRST PARAGRAPH

On pages (2)-(3) of the Office Action, claim 50 was rejected under 35 U.S.C. §112, first paragraph as lacking enablement. Applicants respectfully traverse this rejection because one of skill in the art would not agree with the Patent Office's belief that the technical disclosure in the specification, "while being enabling for the treatment of dyskinesia, does not reasonably provide enablement for the prevention/prophylactic treatment of dyskinesia as recited in claim 50" (as articulated at page 3 of the outstanding Office Action).

As taught in the specification, Applicants have discovered that abnormal patterns of neural activity in a brain region called the basal ganglia are the key underlying cause of dyskinesias. In this context, the specification then teaches that the compounds of the formula (I) as defined in the present claims bind specifically to this part of the brain and stabilize neuronal activity there, thus inhibiting dyskinesia (see, e.g. pages 7-8). The specification further teaches how the compounds of general formula (I) are believed to reduce and prevent dyskinesia (see page 8, final paragraph of the present application), as well as how the compounds are to be administered (see page 18, second paragraph to page 23, fifth paragraph of the present application). Because the specification teaches that abnormal patterns of neural activity in a brain region called the basal ganglia underlie dyskinesias and further that the claimed compounds stabilize neuronal activity in the basal ganglia,

one of skill in the art would not agree with the Patent Office's determination that the skilled artisan would view the use of the claimed compounds for prevention/prophylactic treatment of one or more symptoms of dyskinesia to be "highly unlikely" (Office action page 4, first full paragraph). Instead, those of skill in the art would note Applicants' teaching that abnormal patterns of neural activity in a brain region called the basal ganglia are the key underlying cause of dyskinesias and further that the compounds of the formula (I) as defined in the present claims bind specifically to this part of the brain and stabilize neuronal activity there, thus inhibiting dyskinesia. Since this is the underlying mechanism of dyskinesias, it would be self-evident to the skilled person that the compounds of the formula (I) will prevent dyskinesias whether they are administered after dyskinesia has been established or before dyskinesia appears (i.e. prophylactic). One of skill in this art would therefore view the use of the claimed compounds for prevention/prophylactic treatment of one or more symptoms of dyskinesia to be credible because for example, the technical logic underlying the asserted utility is sound; and the facts upon which the assertion is based is entirely consistent with the logic underlying this assertion.

As noted in M.P.E.P. §2107.02, where an applicant has specifically asserted that an invention has a particular therapeutic utility (e.g. prevention/prophylactic treatment of dyskinesia), that assertion of utility is to be considered credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based is inconsistent with the logic underlying the assertion. As noted above, neither situation occurs in Applicants' asserted utility and the Patent Office further fails to provide evidence sufficient to show that the statement of asserted utility would be considered "false" by a person of ordinary skill in the art. Consequently, the legal presumption that Applicants' statement of therapeutic utility is true has not been overcome by the Patent Office. For this reason, the Patent Office's rejection of claim 50 fails to establish the elements needed for a prima facie rejection under 35 U.S.C. §112 and should therefore be withdrawn.

Applicants' further traverse the rejection to claim 50 because it mistakenly confuses the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption. In particular, in *In re Brana*, 51 F.3d 1560, 34 U.S.P.Q.2d 1436 (Fed. Cir. 1995), the Federal Circuit clearly held that therapeutic utility sufficient under the patent laws is not to be confused with the requirements of the FDA with regard

to safety and efficacy of drugs to obtain market approval in the United States. In *In re Brana*, the Federal Circuit held that the FDA's requirements of testing for safety and effectiveness are not required by the patent laws. The holding in *In re Brana*, follows the well established precedent that:

> [T]he Patent Office has not been charged by Congress with the task of protecting the public against possible misuse of chemical patents. There is nothing in the patent statute or any other statutes called to our attention which gives the Patent Office the right or the duty to require an applicant to prove that compounds or other materials which he is claiming, and which he has stated are useful for "pharmaceutical applications" are safe, **effective** and reliable for use in humans. In re Krimmel, 292 F.2d 948, 952 (CCPA 1962).

For this additional reason, the rejection under 35 U.S.C. §112 should be withdrawn

In summary, because one of skill in the art would not agree with the Patent Office's determination that the use of the claimed compounds for prevention/prophylactic treatment of one or more symptoms of dyskinesia is "highly unlikely", and further because the outstanding rejection is predicated on a requirement that is contrary to case law (e.g. *In re Brana*, and *In re Krimmel*), Applicants respectfully request the withdrawal of the rejection to claim 50 under 35 U.S.C. §112.

V. Prior Art Rejections

On page (6) of the Office Action, claims 26, 27, 30, 33-34, 36-37, 39, and 41-45 were rejected under 35 U.S.C. §103(a) as being unpatentable over Chenard et al., EP 0900568 (Chenard) in view of Ling et al., U.S. Patent No. 6,200,970 (Ling). On page (7) of the Office Action, claims 28, 29, 31 and 32 were rejected under 35 U.S.C. §103(a) as being unpatentable over Chenard in view of Ling as applied to claims 26, 27, 30, 33-34, 36-37, 39, and 41-45 in further view of Solyom et al., "Current Pharmaceutical Design, May 2002," (Solyom). On page (8) of the Office Action, claim 35 was rejected under 35 U.S.C. §103(a) as being unpatentable over Chenard in view of Ling as applied to claims 26, 27, 30, 33-34, 36-37, 39, and 41-45 in further view of http://web.archive.org/web/20000815082545/neurologychannel.com/parkinsondisease/index.shtml.

Applicants respectfully traverse these rejections. In the sections below, Applicants' attorney reviews the invention recited in the claims and the references cited by the Patent Office. Applicants'

attorney then identifies how these references cannot be used to render the invention recited in the claims obvious.

## 1. THE CLAIMED INVENTION AND THE CITED REFERENCES

### A. The Claimed Invention

The invention recited in claim 26 relates to a method of treating dyskinesia in a subject comprising administering to the subject a therapeutically effective amount of a compound of the formula (I) as defined in claim 26. In this context, those of skill in this art understand that dyskinesias are pathologies that are distinct from other movement disorders such as Parkinson's disease. Those of skill in the art further understand that dyskinesias are a common side-effect of agents (such as L-Dopa) that are used to treat Parkinson's disease.

### B. EP 0900568 to Chenard *et al.*

Chenard *et al.* discloses a method of treating dyskinesias resulting from the use of dopamine agonist therapy by administering AMPA receptor antagonists (see page 2, lines 5 and 6 and page 2, line 47 to page 9, line 53 of Chenard *et al.*). As acknowledged by the Examiner at page 6 of the outstanding Office Action, the AMPA receptor antagonists disclosed in Chenard *et al.* do not correspond to the compounds of the formula (I) as defined in claim 26.

### C. U.S. Patent No. 6,200,970 to Ling et al.

Ling *et al.* discloses 8-alkoxy-substituted 2,3-benzodiazepine derivatives and their use as inhibitors of AMPA receptors and in the treatment of neurological disorders that are triggered by the over stimulation of the AMPA receptor (see column 1, lines 17 to 55 and column 2, line 64 to column 3, line 31 of Ling *et al.*).

There is no disclosure in Ling *et al.* of the use of the derivatives it describes in the treatment of dyskinesia, which is different from the neurodegenerative diseases that are the target of the compounds disclosed in Ling *et al.*

2. APPLICANTS' RESPONSE TO THE REJECTIONS UNDER 35 U.S.C. 103(a)

In the outstanding rejection under 35 U.S.C. § 103(a), the Patent Office asserts that because Chenard teaches that a dyskinesia can be treated using the AMPA antagonists disclosed therein, it would have been obvious to the skilled person to treat dyskinesias using all AMPA antagonists known in the art, including those having a completely different chemical formula from the compounds disclosed in Chenard (in this case, those disclosed in Ling).

Applicants respectfully traverse this rejection. As noted for example in KSR v. Teleflex, 550 U.S. ___, 127 S. Ct. 1727 (2007), in determinations of obviousness under 35 U.S.C. §103(a), there must be some motivation to combine references. In this context however, neither Chenard nor Ling teaches or suggests the use of non-AMPA receptor antagonists to treat dyskinesias (much less the specific non-AMPA receptor antagonists that are recited in claim 26). Consequently, the skilled artisan could not have been motivated to mix the pathological syndromes disclosed in Chenard with the chemical compositions disclosed in Ling to generate the invention recited in claim 26. For this reason, Applicants respectfully request a withdrawal of the rejection to claim 26 under 35 U.S.C. §103(a).

Applicants further traverse this rejection because one of skill in the art would not agree with the technical arguments relied upon by the Patent Office to reject claim 26 under 35 U.S.C. § 103(a). In particular, Applicants respectfully traverse this rejection because it disregards the chemistry and pharmacology of the compounds disclosed in Chenard as compared the chemistry and pharmacology of the compounds that are the subject of the present application (e.g. their respective pharmacological profiles *in vivo*). In this context, those of skill in the art understand that the compounds disclosed for example in Ling only have superficial similarities to the compounds of the formula (I) as defined in claim 26. **For example, the skilled artisan will note that the compounds of the formula (I) as defined in claim 26 are a <u>different sub-set of 2,3-benzodiazepines</u> from the AMPA receptor antagonists disclosed in Ling *et al.* and are <u>not AMPA receptor antagonists</u>.**

Because skilled artisans understand that chemical compounds having different structures correspondingly have different pharmacological properties, such artisans would not agree that one would have been motivated to mix and match the disclosures of Chenard and Ling in a manner that produces the invention recited in claim 26 (i.e. as asserted by the Patent Office). For example, a

physician artisan treating a patient suffering from dyskinesia following a therapeutic regimen that called for a chemical compound disclosed in Chenard would not agree that he or she could simply substitute a chemical compound disclosed in Ling because, as the Patent Office asserts, they are "taught to be useful in treating neurodegenerative diseases such as Parkinson's disease". Moreover, a physician artisan who used the Chenard and Ling compounds interchangeably in different therapeutic protocol(s) for which they were approved would likely have their professional competence called into question. For this reason, the skilled artisan would not have found it obvious to combine the Chenard and Ling disclosures in order to generate invention recited in claim 26. For this additional reason, Applicants respectfully request a withdrawal of the rejection to claim 26 under 35 U.S.C. §103(a)

For the reasons noted above, Applicants also traverse the rejection to claims 28-29 and 31-32 as being unpatentable over Chenard in view of Ling as applied to claims 26, 27, 30, 33-34, 36-37, 39, and 41-45 in further view of Solyom. In particular, Solyom merely discusses the structure-activity relationship among AMPA antagonist 2,3-benzodiazepines and provides no teaching that is absent from either Chenard et al. or Ling et al. that would have been required in order for the skilled person reading these documents to arrive at the invention as defined in claim 26. Consequently, Solyom fails to remedy the deficiencies in the Chenard and Ling disclosures.

In addition, in the outstanding obviousness rejection that is predicted on a combination of Chenard, Ling and Solyom, Patent Office asserts that Solyom et al. teaches 2,3-benzodiazepine derivatives, specifically Tofisopam, as non-competitive AMPA antagonists. One of skill in the art will note that this characterization of the Solyom disclosure is not correct. Instead, one of skill in the art will note that Solyom et al. specifically states that **Tofisopam is an example of a 2,3-benzodiazepine compound that is <u>not</u> an AMPA antagonist** (see Chart 2 on page 917 and the paragraph bridging pages 920 and 921 of Solyom et al.). In this context and as discussed above, the skilled person reading Chenard et al. and Ling et al. would have been actively discouraged from using a compound, such as Tofisopam, that is not an AMPA antagonist to treat dyskinesia. This disclosure in Solyom in combination with Chenard and Ling therefore could not have led the skilled person to select a compound of formula (I) as defined in claim 26 for the treatment of dyskinesia. Thus, claims 26 to 50 are non-obvious over the disclosures of Chenard, Ling and Solyom. For these

reasons, Applicants respectfully request a withdrawal of the rejection to claims 26, 27, 30, 33-34, 36-37, 39, and 41-45 under 35 U.S.C. §103(a).

For the reasons noted above, Applicants also traverse the rejection to claim 35 as being unpatentable over Chenard in view of Ling as applied to claims 26, 27, 30, 33-34, 36-37, 39, and 41-45 in further view of http://web.archive.org/web/20000815082545/neurologychannel.com/parkinsondisease/index.shtml.

As discussed above, the subject matter in claim 35 is non-obvious over the disclosures of Chenard et al. and Ling et al. by virtue of its dependency on claim 26.

Moreover, those of skill in this art will note that the "PD Website" is nothing more than a common, superficial dictionary description of Parkinson's disease. It provides no teaching of relevance to the presently claimed invention and certainly provides no teaching or suggestion to use a compound of the formula (I) to treat dyskinesias, let alone to specifically treat dyskinesias associated with idiopathic Parkinson's disease. Thus, claims 26 to 50 are non-obvious over the disclosures of Chenard et al., Ling et al. and the "PD Website".

Thus, independent claim 26 is allowable over Chenard and Ling, either alone, or in combination with other disclosures such as those found in Solyom and/or a "PD website". Further, the dependent claims are submitted to be allowable over these disclosures in the same manner, because they are dependent on independent claim 26 and thus contain all the limitations of these independent claims. In addition, the dependent claims further recite constellations of novel elements not shown by Chenard, Ling, Solyom and/or the "PD website".

## VI. Conclusion

In view of the above, it is submitted that this application is now in good order for allowance and such allowance is respectfully solicited. Should the Examiner believe minor matters still remain that can be resolved in a telephone interview, the Examiner is urged to call Applicants' undersigned attorney.

The Commissioner is hereby authorized to charge Deposit Account NO. 50-0494 in the amount of $130.00 for a one-month extension of time. Please also charge any necessary additional fees, or credit any overpayments, to Gates & Cooper LLP Deposit Account No. 50-0494.

Respectfully submitted,

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